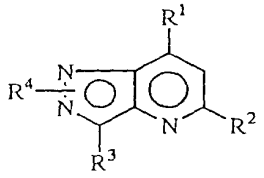
Claims

1. Use of compounds of formula (I)



(I),

including the stereoisomers and the pharmaceutically acceptable acid addition salt forms thereof, wherein

R^1 is C_{1-6}alkyl, NR^5R^6, OR^6 or SR^6;

R^2 is C_{1-6}alkyl, C_{1-6}alkyloxy, or C_{1-6}alkylthio;

R^3 is Ar^1 or Het^1;

R^4 is hydrogen or C_{1-6}alkyl;

R^5 is hydrogen, C_{1-8}alkyl, mono- or di(C_{3-6}cycloalkyl)methyl, C_{3-6}cycloalkyl, C_{3-6}alkenyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyloxyC_{1-6}alkyl, mono- or di(C_{1-6}alkyl)aminoC_{1-6}alkyl or C_{1-6}alkyloxyC_{1-6}alkyl;

R^6 is C_{1-8}alkyl, mono- or di(C_{3-6}cycloalkyl)methyl, Ar^2C_{1-6}alkyl, Ar^2oxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{3-6}alkenyl, thienylmethyl, furanylmethyl, tetrahydrofuranylmethyl, C_{1-6}alkylthioC_{1-6}alkyl, mono- or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, di(C_{1-6}alkyl)amino, or C_{1-6}alkylcarbonylC_{1-6}alkyl;

or R^5 and R^6 taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, homopiperidinyl, morpholinyl, or thiomorpholinyl group, optionally substituted with 1 or 2 substituents each independently selected from C_{1-6}alkyl or C_{1-6}alkyloxyC_{1-6}alkyl;

Ar^1 is phenyl; naphtyl; or phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C_{1-6}alkyl, trifluoromethyl, hydroxy, cyano, C_{1-6}alkyloxy, benzyl, benzyloxy, C_{1-6}alkylthio, nitro, amino and mono- or di(C_{1-6}alkyl)amino;

Het^1 is pyridinyl; pyridinyl substituted with 1, 2 or 3 substituents each independently selected from halo, C_{1-6}alkyl, trifluoromethyl, hydroxy, cyano, C_{1-6}alkyloxy, benzyloxy, C_{1-6}alkylthio, nitro, amino, and mono- or di(C_{1-6}alkyl)amino; and

Ar^2 is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, hydroxy, C_{1-6}alkyl, C_{1-6}alkyloxy, di(C_{1-6}alkyl)aminoC_{1-6}alkyl, or trifluoromethyl; or pyridinyl;

for the manufacture of a medicament for treating physiological conditions or disorders arising from the hypersecretion of corticotropin-releasing factor (CRF).

2. Use of a compound according to claim 1 wherein R^1 is NR^5R^6 wherein R^5 is hydrogen or C_{1-8}alkyl; and R^6 is C_{1-8}alkyl or C_{3-6}cycloalkylmethyl; or R^1 is OR^6 or SR^6 wherein R^6 is C_{1-6}alkyl; R^2 is C_{1-6}alkyl; R^3 is a phenyl substituted with 1, 2 or 3 substituents each independently selected from C_{1-6}alkyl, C_{1-6}alkyloxy or halo; or R^3 is a pyridinyl substituted with 1, 2 or 3 substituents each independently selected from halo, amino, nitro, trifluoromethyl, mono- or di(C_{1-6}alkyl)amino, or C_{1-6}alkyl; and R^4 is hydrogen or C_{1-6}alkyl.

3. A compound of formula (I-1) wherein R^1 to R^4 are defined as in claim 1 and wherein

at least R^1 is C_{1-6}alkyl; OR^6; SR^6; or NR^5R^6 wherein R^5 is mono- or di(C_{3-6}cycloalkyl)methyl, C_{3-6}cycloalkyl, C_{3-6}alkenyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyloxyC_{1-6}alkyl, mono- or di(C_{1-6}alkyl)aminoC_{1-6}alkyl or C_{1-6}alkyloxyC_{1-6}alkyl, and R^6 is mono- or di(C_{3-6}cycloalkyl)methyl, Ar^2C_{1-6}alkyl, Ar^2oxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkyl, C_{3-6}alkenyl, thienylmethyl, furanylmethyl, tetrahydrofuranylmethyl, C_{1-6}alkylthioC_{1-6}alkyl, C_{1-6}alkylcarbonylC_{1-6}alkyl, mono- or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, or di(C_{1-6}alkyl)amino; or R^5 and R^6 taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, or homopiperidinyl, each substituted with 1 or 2 substituents independently selected from C_{1-6}alkyl or C_{1-6}alkyloxyC_{1-6}alkyl; or R^5 and R^6 taken together with the nitrogen atom to which they are attached may form a morpholinyl or a thiomorpholinyl group, optionally substituted with 1 or 2 substituents independently selected from C_{1-6}alkyl or C_{1-6}alkyloxyC_{1-6}alkyl; or

at least R^3 is Het^1 or Ar^1 wherein Ar^1 is naphtyl; or phenyl substituted with 3 substituents each independently selected from halo, C_{1-6}alkyl, trifluoromethyl, hydroxy, cyano, C_{1-6}alkyloxy, benzyl, benzyloxy, C_{1-6}alkylthio, nitro, amino and mono- or di(C_{1-6}alkyl)amino.

4. A compound according to claim 3 wherein R^1 is a radical of formula NR^5R^6 wherein R^5 is mono- or di(C_{3-6}cycloalkyl)-methyl, C_{3-6}cycloalkyl, C_{3-6}alkenyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyloxyC_{1-6}alkyl, mono- or di(C_{1-6}alkyl)amino-C_{1-6}alkyl or C_{1-6}alkyloxyC_{1-6}alkyl, and R^6 is mono- or di(C_{3-6}cycloalkyl)methyl, Ar^2C_{1-6}alkyl, Ar^2oxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkyl, C_{3-6}alkenyl, thienylmethyl, furanylmethyl, tetrahydrofuranylmethyl, C_{1-6}alkylthioC_{1-6}alkyl, C_{1-6}alkylcarbonylC_{1-6}alkyl, mono- or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, or di(C_{1-6}alkyl)amino.

5. A compound according to claim 3 wherein R^1 is a radical of formula NR^5R^6 whereinor R^5 and R^6 taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, or homopiperidinyl, each substituted with 1 or 2 substituents independently selected from C_{1-6}alkyl or C_{1-6}alkyloxyC_{1-6}alkyl; or R^5 and R^6 taken together with the nitrogen atom to which they are attached may form a morpholinyl or a thiomorpholinyl group, optionally substituted with 1 or 2 substituents independently selected from C_{1-6}alkyl or C_{1-6}alkyloxyC_{1-6}alkyl.

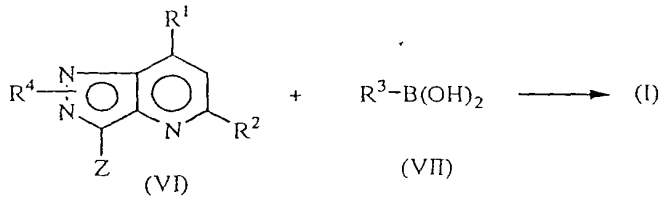
6. A compound according to claim 3 wherein R^3 is Het^1 or Ar^1 wherein Ar^1 is naphtyl; or phenyl substituted with 3 substituents each independently selected from halo, C_{1-6}alkyl, trifluoromethyl, hydroxy, cyano, C_{1-6}alkyloxy, benzyl, benzyloxy, C_{1-6}alkylthio, nitro, amino or mono- or di(C_{1-6}alkyl)amino.

7. A composition comprising a pharmaceutically acceptable carrier, and as active ingredient a therapeutically effective amount of a compound as claimed in any one of claims 3 to 6.

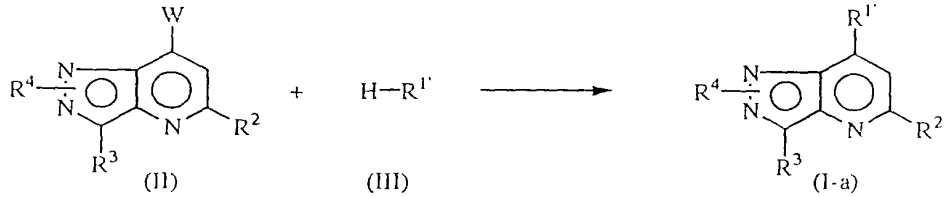
8. A process for preparing a composition as claimed in claim 7 wherein a therapeutically effective amount of a compound as claimed in any one of claims 3 to 6 is intimately mixed with a pharmaceutically acceptable carrier.

9. A compound according to any one of claims 3 to 6 for use as a medicine.

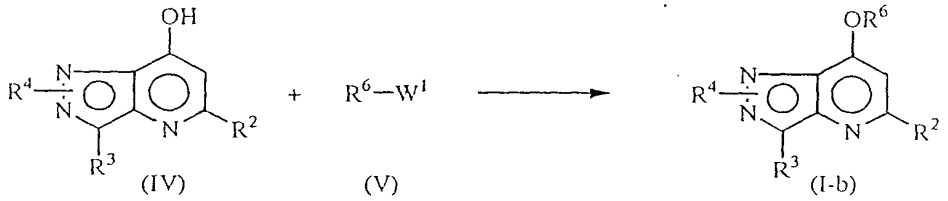
10. A process of preparing a compound of formula (I-1) as claimed in claim 3 wherein
a) intermediates of formula (VI) are reacted with intermediates of formula (VII) under Suzuki coupling conditions;



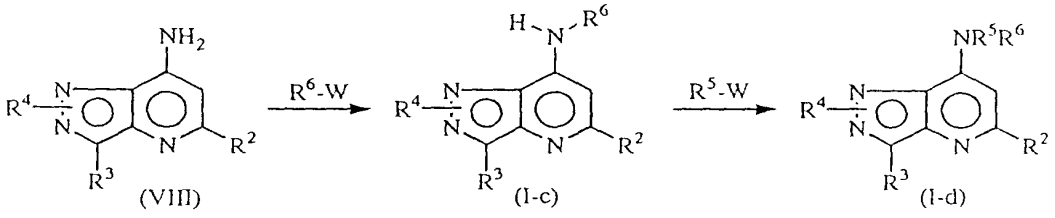
b) an intermediate of formula (II) is reacted with an intermediate of formula (III), wherein $R^{1'}$ has the meaning of R^1 other than C_{1-6}alkyl, thereby yielding compounds of formula (I-a);



c) an intermediate of formula (IV) is *O*-alkylated with an intermediate of formula (V) in a reaction-inert solvent and in the presence of a suitable base, yielding compounds of formula (I-b), defined as compounds of formula (I) wherein R^1 is OR^6,



d) an intermediate of formula (VII) is *N*-alkylated with an intermediate of formula R^6-W in a reaction-inert solvent and in the presence of a suitable base, yielding compounds of formula (I-c), which can be further *N*-alkylated with an intermediate of formula R^5-W



wherein in the above reaction schemes the radicals R^1 to R^6, are as defined in claim 1, Z is bromo or iodo and W and W^1 are appropriate leaving groups;

or, if desired, compounds of formula (I) are converted into each other following art-known transformation reactions; and further, if desired, compounds of formula (I) are converted into an acid addition salt by treatment with an acid, or conversely, the acid addition salt forms are converted into the free base by treatment with alkali; and, if desired, preparing stereochemically isomeric forms thereof.